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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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YANN ECHELARD

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2099

7590

08/27/2002

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EXAMINER

WOITACH, JOSEPH T

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 08/27/2002

20

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/298,508

Applicant(s)

ECHELARD ET AL.

Examiner

Joseph Woitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31,34-44,47-58,60,61,65-73,86-88 and 90-95 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

- 5) ☐ Claim(s) _____ is/are allowed.

- 6) ☒ Claim(s) 31,34-44,47-58,60,61,65-73,86-88 and 90-95 is/are rejected.

- 7) ☐ Claim(s) _____ is/are objected to.

- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.

- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some * c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.

4) ☐ Interview Summary (PTO-413) Paper No(s). _____.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other:

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Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 12, 2002, paper number 19, has been entered.

DETAILED ACTION

This application filed April 22, 1999, claims benefit to provisional application 60/106,728, filed November 2, 1998.

As indicated in Applicants request for RCE, the after final amendment filed January 4, 2002, paper number 16, has been entered. Claims 1, 4-14, 17-28 and 30 have been canceled. Claims 31, 40, 44, 56-58, 61 and 91 have been amended. Claims 92-95 have been added. Claims 31, 34-44, 47-58, 60, 61, 65-73, 86-88 and 90-95 are pending and currently under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

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The oath or declaration is defective because: the full name of Esmail Behbodi is misspelled and does not match the signature Esmail Behboodi.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31, 34-44, 47-58, 60, 61, 65-73, 86-88 and 90-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a preparation of embryonic or fetal cells derived from a normal or transgenic goat, does not reasonably provide enablement for said cells isolated from a goat in which an endogenous gene has been specifically disrupted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by

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weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant invention is drawn to purified preparations of embryonic or fetal caprine somatic cells and methods of making said cells. The specification provides for methods readily known in the art for the isolation of said cells from an embryo or fetus. Normal and transgenic goats are known and taught in the art, however, goats with specific alterations in an endogenous gene are not. The basis of the instant rejection is based on the lack of a goat that contains a disruption in its genome, and the failure of the specification to teach the methods necessary to generate such a goat. Specifically, claims 36, 48 and 66 recite and encompass goats which have knock-out or knock-in constructs, and thus, independent claims also encompass this limitation. Presently, for the methodology for the generation of animals with knock-out constructs requires the existence of totipotent embryonic stem cells. Presently, the art does not teach that such a cell exist for a goat (see for example Wells *et al.* Biology of Reproduction, Echelard Curr. Opinion in Biotech.). Further, the present specification is silent with respect to methods of generating goat embryonic stem cells or alternative methods for generating knock-out/in goats. The specification

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provides art recognized methods for isolating cells that already exist, however the specification fails to provide the necessary guidance for generating new animals, in particular goats with specific alterations in its genome. Without such guidance in the specification and the lack of correlative teaching or working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan. Because the specification provides no guidance or teaching on how to affect the presently claimed products or methods of use, the instantly claimed products and methods are not enabled for the full breadth of the claim. The courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application. *Ex parte Maizel*, 27 USPQ2d 1662.

The instant invention, as claimed, falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genentech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005). The claimed methods of transfer constitute such a "germ of an idea".

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In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31, 34-44, 47-58, 60, 61, 65-73, 86-88 and 90-95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 31 is vague and unclear in the recitation of "derived from a germ cell" because what is encompassed by derived is not clearly set forth. The process on how a embryonic or fetal goat is "derived" is unclear, therefore the metes and bounds of the claim can not be defined.

Claim 34 is unclear and confusing in the recitation "the transgene is a heterologous transgene" because it is not clear how this further limits the transgene. All transgenes do not exist naturally, therefore they are all heterologous.

Claims 36, 48 and 66 are confusing because independent claims indicate that the transgene was expressed in the transgenic, however knock-out/knock-in constructs abolish the expression of a targeted gene. The limitation of this claim is not consistent with the independent and thus is an improper dependent claim because it does not further limit the independent claim.

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Claim 31 and other dependent claims are included in the basis of the rejection because they embody and fail to clarify the specific rejections set forth above.

Claims 92 and 94 are vague and unclear because the nature of the cell which is isolated on or after day 10 is exactly the same as that isolated at any time during embryogenesis. Claim 31 and 44 are not methods and it is unclear how claims 92 and 94 would further limit the cell of claims 31 or 44.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

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Claims 31, 34, 35, 37, 42-44, 47, 49, 54-58, 61, 65, 67, 72, 73, 86-88 and 90-95 are rejected under 35U.S.C. 102(b) as being anticipated by Archer *et al.*

Applicants point out that the claims are drawn to cells in which the transgenes were expressed in a transgenic goat. Further, Applicants point out certain features that these cells may have. Applicants argue that instantly claimed cells are distinguishable from that of Archer *et al.* and that the transgene inserted by retrovirus may represent several copies and may not be expressed under certain circumstances when used for cloning. Applicants argue that isolating cells from an animal that has demonstrated transgene expression represents a more desirable cell phenotype that Archer *et al.* does not teach. See Applicants' amendment, pages 9-10.

Applicants arguments have been fully considered, but not found persuasive.

As noted in the previous rejection, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*. Whether the rejection is based on "inherency" under 35 USC 102, on "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

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First, in the construction of transgenic animals, often multiple copies of gene are present in the transgenic animal, therefore arguments that the retrovirus will introduce multiple copies is not persuasive. Second, the cells taught by Archer *et al.* do express the transgene that was transduced, therefore arguments that the cells might not express the transgene are not found persuasive. The instant invention draws from recent success in the art for cloning farm animals by nuclear transfer methodology. The present specification does not provide any novel methodology which was not previously taught in the art for isolating somatic cells from a normal animal, or more specifically from a fetal goat, only that these cells provide the basis for cloning the transgenic goats given the current technology.

With respect to newly added claims 92 and 94, the limitation of obtaining a cell on or after day 10 do not appear to change the specific nature of cell isolated. With respect to claims 93 and 95, MPEP 2144.04 states "The court found that matters relating to ornamentation only which have no mechanical function cannot be relied upon to patentably distinguish the claimed invention from the prior art." See *In re Seid*, 161 F.2d 229, 73 USPQ 431 (CCPA 1947). In the instant case, simply putting the cells in a container does not distinguish cells from those previously taught in the art.

Claims 31, 34, 35, 37, 42-44, 47, 49, 54-58, 61, 65, 67, 72, 73, 86-88 and 90-95 are rejected under 35U.S.C. 102(e) as being anticipated by Strelchenko *et al.*

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Applicants summarize the previous rejection and point out that instantly claimed methods are drawn to preparing embryonic or fetal goat somatic cell lines. Applicants argue that the methods taught by Strelchenko *et al.* does not anticipate the instantly claimed methods. See Applicants amendment, pages 10-12. Applicants' arguments have been fully considered, but not found persuasive.

First, it is noted that products encompassed by claim 31 are drawn to preparations of cells "derived from the germ cell of a transgenic goat" and that claims 61 drawn to methods for isolation also recite "derived from the germ cell of a transgenic goat". Step (a) of claim 61 recites broadly recites the open language of "obtaining" and thus, is not limited to any particular method of obtaining an embryo or a fetus. Thus, ability to derive a cell from the totipotent stem cell clearly anticipates the instant claims. Further, the instant claims do not recite limitations that the transgene must be present in both chromosomes, and fairly reads on a cell with one transgene copy. Strelchenko *et al.* teach methods for observing transgene behavior during embryogenesis and methods to obtain cells from embryos for this purpose. The fact that Strelchenko *et al.* do not actually reduce to practice goat somatic cells is no matter because working examples are not required to demonstrate all operable embodiments of an invention. The disclosure of Strelchenko *et al.* provide the necessary guidance to derive fetal somatic cells from a developing embryo to analyze transgene behavior, and therefore anticipate the instantly claimed products and methods to isolated said products.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 31, 34, 35, 37-44, 47, 49-58, 60, 65, 67, 72, 73, 86-88 and 90-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Archer *et al.* and Amoah *et al.*

Applicants note that even if the transgene introduced by a retrovirus is integrated into the genome, the instantly claimed cells are distinguished from those of Archer *et al.* because they are isolated from a transgenic goat and therefore, provide the desirable qualities for use in generating transgenic goats. Further, it is argued that the methods taught in Amoah *et al.* do not compensate the deficiencies of Archer *et al.* See Applicants' amendment, page 13. Applicants arguments have been fully considered, but not found persuasive.

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As noted above, the teaching of Archer *et al.* provide the necessary guidance and teaching which anticipates the limitations broadly encompassed by the present claims. As noted in the previous office actions, the teaching of Amoah *et al.* relied upon in the instant rejection is the demonstration of the skill and state of the act, in particular the use of various promoters and transgenes in the construction of transgenic animals. Further, the transgenic goats taught in Amoah *et al.* represent the transgenic goats which Applicants have argued are the unique source for the instantly claimed products. The instant invention relies on the transgenic goats which exist at the time of filing, and the teaching of Amoah *et al.* provide the basis for transgenic goats and the specific promoters and transgenes used in their construction. Amoah *et al.* provide evidence that transgenic goats and the cells which inherently exist within these animals could be generated, and the teaching of the specific promoters and genes therein, while the teaching of Archer *et al.* provide another means to produce the cells which are instantly claimed.

Thus, for the reasons above and of record the claimed invention as a whole was *prima facie* obvious.

Claims 31, 34-44, 47-58, 60, 61, 65-73, 86-88 and 90-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Archer *et al.* and Amoah *et al.* in further view of Strelchenko *et al.*

Applicants present arguments for the deficiencies of each reference as presented above in traverse of the 102 rejections. Further, it is argued that the methods taught in Amoah *et al.* do

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not compensate the deficiencies of Archer *et al.* or Strelchenko *et al.* See Applicants amendment, pages 14-15. Applicants' arguments have been fully considered, but not found persuasive.

As noted above, the instant invention draws from recent success in the art for cloning farm animals by nuclear transfer methodology. The present specification does not provide any novel methodology which was not previously taught in the art for isolating somatic cells from a normal animal, or more specifically from a fetal goat, only that these cells provide the basis for cloning the transgenic goats given the current technology. Archer *et al.* provide one means of generating transgenic goats wherein the transgene is introduced by a retrovirus. Strelchenko *et al.* provide the use of more traditional methods for generating wholly transgenic animals. Each Archer *et al.* and Strelchenko *et al.* provide the necessary teaching for the generation of transgenic animals and specifically provide methods for providing somatic cells to access transgene expression. Amoah *et al.* provide a teaching of the various promoters and transgenes used in generating transgenic goats. Clearly, each of the references are related in their teaching for generating transgenic goats. Further, in view of the teaching of Strelchenko *et al.* for the analysis of transgene expression in developing embryos, and the teaching of Archer *et al.* for the generation of transgenic somatic cells and the general teaching of Amoah *et al.*, the instantly broadly claimed cells and methods of obtaining said cells would have been obvious to one of ordinary skill in the art at the time of the claimed invention. Because the references provide working examples of what had been made in the art there would have been a reasonable

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expectation of success to obtain these cells, and to generate other cells with any promoter or transgene known to work in transgenic animals.

Thus, for the reasons above and of record the claimed invention as a whole was *prima facie* obvious.

Conclusion

No claim is allowed.

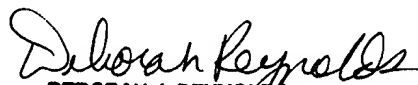
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach


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